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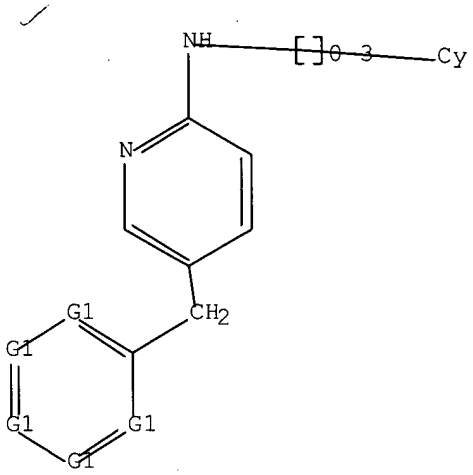


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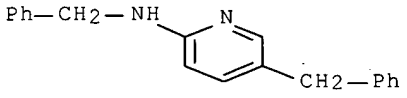
L5   ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   1999:83141  CAPLUS  Full-text
DN   130:209581
TI   Acid-catalyzed N-debenzylation of (benzylamino)pyridines
AU   Kowalski, P.; Majka, Z.; Kowalska, T.
CS   Institute of Organic Chemistry and Technology, Cracow University of
     Technology, Krakow, 31-133, Pol.
SO   Chemistry of Heterocyclic Compounds (New York)(Translation of Khimiya
     Geterotsiklicheskikh Soedinenii) (1998), 34(6), 740-741
     CODEN: CHCCAL; ISSN: 0009-3122
PB   Consultants Bureau
DT   Journal
```

LA English
OS CASREACT 130:209581
AB Several 2- and 4-(benzylamino)pyridines, 2,6-bis(benzylamino)pyridine, and 2-(benzylamino)quinoline underwent N-debenzylation in 95% H2SO4. Yields were 73-85%. The reaction failed with 3-(benzylamino)pyridine.
IT 137002-80-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(acid-catalyzed N-debenzylation of)
RN 137002-80-3 CAPLUS
CN 2-Pyridinamine, N,5-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:545594 CAPLUS Full-text
DN 129:148914
TI Preparation of 2-amino-4-aryl-5-arylmethyl-5-cyclopentyl-3-hydroxymethylpyridines and related compounds for treatment of arteriosclerosis.
IN Schmeck, Carsten; Brandes, Arndt; Loegers, Michael; Schmidt, Gunter; Bremm, Klaus-Dieter; Bischoff, Hilmar; Schmidt, Delf; Schuhmacher, Joachim
PA Bayer A.-G., Germany
SO Ger. Offen., 22 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

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PI	DE 19704243	A1	19980806	DE 1997-19704243	19970205 <--
	CA 2279636	A1	19980813	CA 1998-2279636	19980123 <--
	WO 9834920	A1	19980813	WO 1998-EP362	19980123 <--
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	AU 730109	B2	20010222		
	BR 9807181	A	20000125	BR 1998-7181	19980123 <--
	EP 973744	A1	20000126	EP 1998-904126	19980123 <--
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	JP 2001510478	T	20010731	JP 1998-533691	19980123
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	BG 103631	A	20001130	BG 1999-103631	19990803
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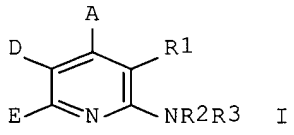
PRAI DE 1997-19704243 A 19970205
WO 1998-EP362 W 19980123
OS MARPAT 129:148914
GI



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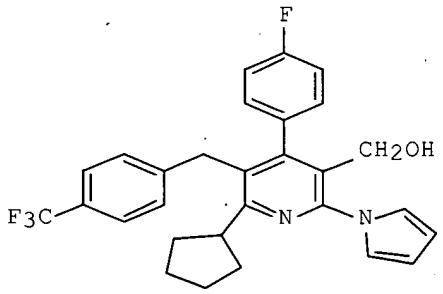
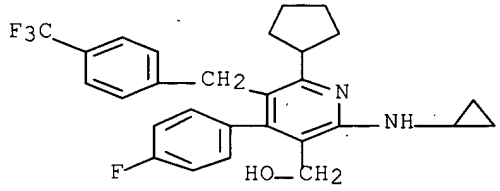


II

AB Title compds. [I; A = (substituted) aryl; D = (substituted) aryl, R6L, etc.; R6 = (substituted) cycloalkyl, aryl, (benzocondensed) mono-, di-, or tricyclic heterocyclyl; L = (substituted) alkyl, alkenyl; E = cycloalkyl, (substituted) alkyl; R1 = hydroxyalkyl; R2, R3 = H, Ph, PhCH2, cycloalkyl, alkyl, acyl, aminocarbonyl; R2R3N = 5-7 membered (unsatd.) (benzocondensed) (substituted) heterocyclyl], were prepared Thus, title compound (II) inhibited cholesteryl ester transfer protein with IC50 = 6 + 10-8 M.

IT 210981-29-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-amino-4-aryl-5-arylmethyl-5-cyclopentyl-3-hydroxymethylpyridines and related compds. for treatment of arteriosclerosis)

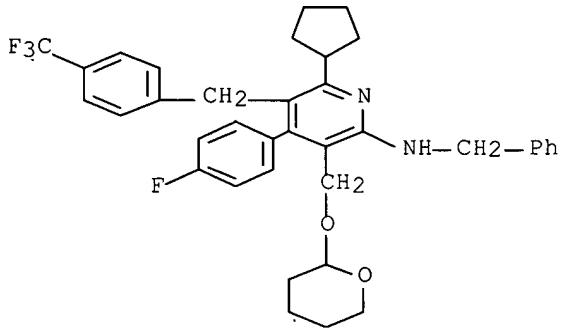
RN 210981-29-6 CAPLUS
CN 3-Pyridinemethanol, 6-cyclopentyl-2-(cyclopropylamino)-4-(4-fluorophenyl)-5-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



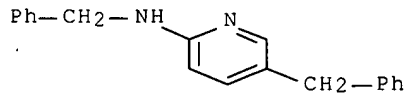
IT 210981-42-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-amino-4-aryl-5-arylmethyl-5-cyclopentyl-3-hydroxymethylpyridines and related compds. for treatment of arteriosclerosis)

RN 210981-42-3 CAPLUS
CN 2-Pyridinamine, 6-cyclopentyl-4-(4-fluorophenyl)-N-(phenylmethyl)-3-

[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-5-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:243760 CAPLUS Full-text
DN 120:243760
TI Action of benzyl chloride on 2-(dimethylamino)pyridine and 2-benzoylaminopyridine
AU Kowalski, Piotr
CS Inst. Org. Chem. Technol., Cracow Univ. Technol., Krakow, 31-155, Pol.
SO Journal of Heterocyclic Chemistry (1994), 31(1), 245-7
CODEN: JHTCAD; ISSN: 0022-152X
DT Journal
LA English
AB The results of the reaction of 2-(dimethylamino)pyridine and 2-(benzoylamino)pyridine with benzyl chloride proved that benzyl chloride did not undergo direct reaction with the pyridine ring to form a C-benzyl product.
IT 137002-80-3P, 2-Pyridinamine, N,5-bis(phenylmethyl)-
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, by benzylation of pyridinamine via ionic intermediates)
RN 137002-80-3 CAPLUS
CN 2-Pyridinamine, N,5-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



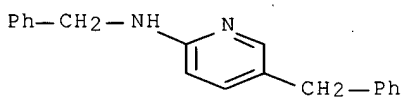
L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:163916 CAPLUS Full-text
DN 120:163916
TI Electrophilic benzylation of the pyridine ring. Action of benzyl chlorides on 2-amino and 2-benzylaminopyridine
AU Kowalski, Piotr
CS Inst. Org. Chem. Technol., Polytech. Univ., Krakow, 31-155, Pol.
SO Journal of Heterocyclic Chemistry (1993), 30(2), 403-8
CODEN: JHTCAD; ISSN: 0022-152X
DT Journal
LA English
OS CASREACT 120:163916

AB The reaction of 2-aminopyridine as well as 2-benzylaminopyridine hydrochloride with benzyl chlorides used in molar ratio of 1:2 and 1:1 resp. and carried out 15 250° leads via 2-benzylamino-5- benzylpyridines to 2-amino-5-benzylpyridines as the final products. The formation of 2-benzylamino-5-benzylpyridines did not occur in the direct C-benzylation reaction of the 2-benzylaminopyridine ring with the use of benzyl chloride. Its formation takes place via the intermediate state of 2-(N,N-dibenzylamino)pyridinium and 1-benzyl-2-benzylaminopyridinium chlorides for which the solvent separated ion-mol. form is proposed. Interaction of the ingredients of the intermediate state i.e., benzyl cation and 2-benzylaminopyridine, leads to an electrophilic mechanism to the formation of 2-benzylamino-5-benzylpyridine hydrochlorides. Thermolysis of the aminomethylene bond in 2-benzylamino-5-benzylpyridine hydrochlorides leads to the final 2-amino-5-benzylpyridines.

IT 137002-80-3P 153373-97-8P 153373-98-9P
153374-01-7P 153374-02-8P 153374-05-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

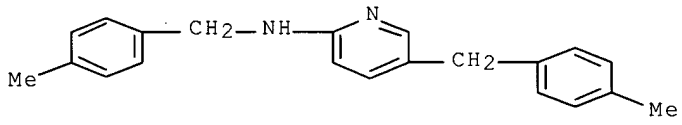
RN 137002-80-3 CAPLUS

CN 2-Pyridinamine, N,5-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



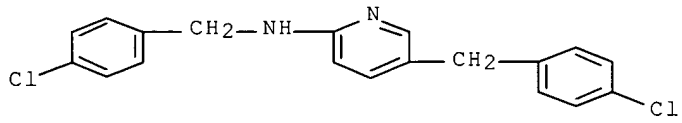
RN 153373-97-8 CAPLUS

CN 2-Pyridinamine, N,5-bis[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



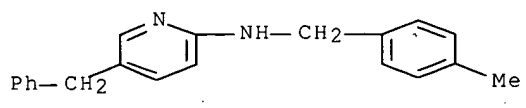
RN 153373-98-9 CAPLUS

CN 2-Pyridinamine, N,5-bis[(4-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)

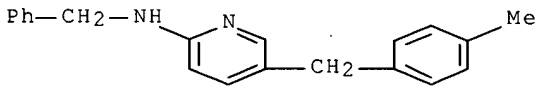


RN 153374-01-7 CAPLUS

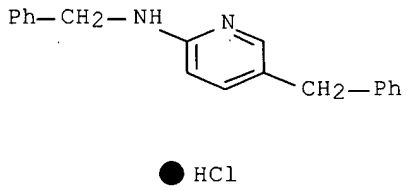
CN 2-Pyridinamine, N-[(4-methylphenyl)methyl]-5-(phenylmethyl)- (9CI) (CA INDEX NAME)



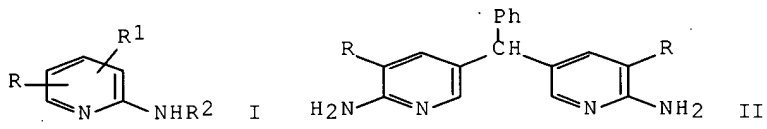
RN 153374-02-8 CAPLUS
CN 2-Pyridinamine, 5-[(4-methylphenyl)methyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 153374-05-1 CAPLUS
CN 2-Pyridinamine, N,5-bis(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

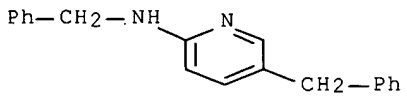


L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1991:632036 CAPLUS Full-text
DN 115:232036
TI Electrophilic benzylation of 2-aminopyridine ring
AU Kowalski, Piotr
CS Inst. Org. Chem. Technol., Politech. Univ., Krakow, 31-155, Pol.
SO Journal of Heterocyclic Chemistry (1991), 28(4), 875-9
CODEN: JHTCAD; ISSN: 0022-152X
DT Journal
LA English
GI

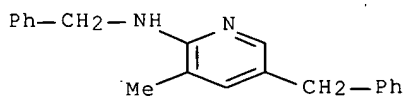


AB Electrophilic benzylation of 2-aminopyridines I (R = H, 3-Me, 5-Me, R1 = R2 = H) gave various benzylated derivs. Thus, I (R = R1 = R2 = H) reacted with PhCH2Cl to give I (R = R1 = H, R2 = CH2Ph; R = H, R1 = 5-CH2Ph, R2 = CH2Ph; R = R2 = H, R1 = 5-CH2Ph) and bis(aminopyridyl)phenylmethane II (R = H). I (R = 3-Me, R1 = R2 = H) reacted with PhCH2Cl to give I (R1 = 5-CH2Ph, R2 = CH2Ph; R1 = 5-CH2Ph, R2 = H) and II (R = Me). Similarly, I (R = 5-Me, R1 = R2 = H) gives I (R1 = H, R2 = CH2Ph; R1 = 3-CH2Ph, R2 = CH2Ph; R1 = 3-CH2Ph, R2 = H).
IT 137002-80-3P
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and electrophilic benzylation of hydrochloride salt of)
RN 137002-80-3 CAPLUS
CN 2-Pyridinamine, N,5-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



IT 137002-81-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 137002-81-4 CAPLUS
CN 2-Pyridinamine, 3-methyl-N,5-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1988:94401 CAPLUS Full-text
DN 108:94401
TI Preparation and formulation of 3-hydroxypyridines useful as histamine H1-antagonists
IN Cooper, David Gwyn; Miles, Peter Donald; Young, Rodney Christopher
PA Smith Kline and French Laboratories Ltd., UK
SO Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

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PI	EP 244201	A2	19871104	EP 1987-303741	19870428 <--
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	AU 8772425	A	19871105	AU 1987-72425	19870501 <--
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OS MARPAT 108:94401
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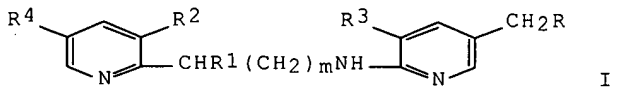


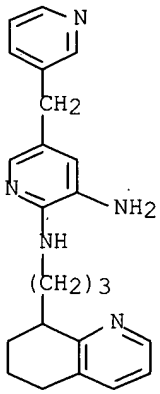
I

AB Title compds. I (R = 2-, 3-, or 4-pyridyl (oxide), (un)substituted N-C1-4 alkylpyridone; R1 = H or with R2 = (CH2)n where n = 2-4; R2 = H, C1-4 alkyl, halo, H2N; R3 = HO, phosphate; R4 = H, C1-4 alkyl, halo, H2N; m = 2-4; and their salts, are prepared 2-Chloro-3-nitro-5-(3- pyridylmethyl)pyridine-HCl prepared in 4 steps from 5-bromo-2- methoxypyridine, was substituted with 4-(5-bromo-3-methyl-2- pyridyl)butylamine to give the nitro(pyridylmethyl)pyridine derivative which was reduced to the amino derivative, this in turn was diazotized to the triazolopyridine derivative which was decomposed to give I (R = 3-pyridyl; R1 = H; R2 = Me; R3 = HO; R4 = Br; m = 4) (II). In tests in vitro and in vivo, II inhibited histamine-mediated guinea pig ileal spasm and bronchoconstriction. An injectable solution (1-5% weight/weight) in vials containing each 2 mL, comprised II and H2O.

IT 112860-46-5P 112878-49-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and diazotization of, triazolopyridine by)

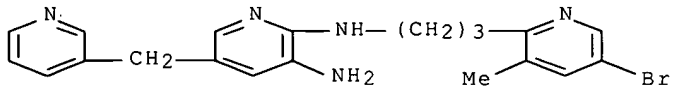
RN 112860-46-5 CAPLUS

CN 2,3-Pyridinediamine, 5-(3-pyridinylmethyl)-N2-[3-(5,6,7,8-tetrahydro-8-quinolinyl)propyl]- (9CI) (CA INDEX NAME)



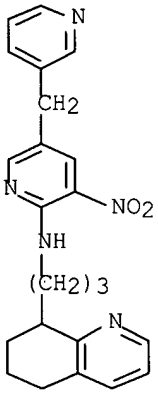
RN 112878-49-6 CAPLUS

CN 2,3-Pyridinediamine, N2-[3-(5-bromo-3-methyl-2-pyridinyl)propyl]-5-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



IT 112860-45-4P 112860-52-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reduction of)
RN 112860-45-4 CAPLUS
CN 8-Quinolinepropanamine, 5,6,7,8-tetrahydro-N-[3-nitro-5-(3-pyridinylmethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 112860-52-3 CAPLUS
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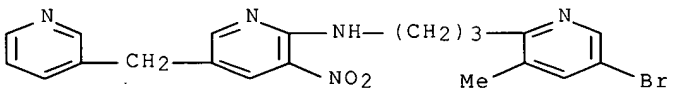
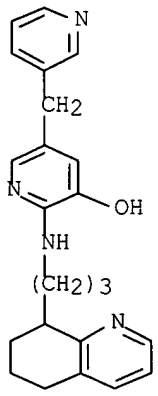
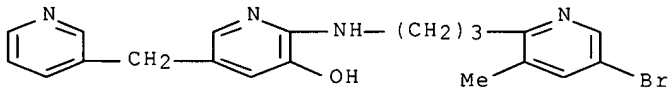


IT 112860-47-6P 112860-54-5P 112860-56-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as histamine antagonist)
RN 112860-47-6 CAPLUS
CN 3-Pyridinol, 5-(3-pyridinylmethyl)-2-[[3-(5,6,7,8-tetrahydro-8-quinolinyl)propyl]amino]- (9CI) (CA INDEX NAME)

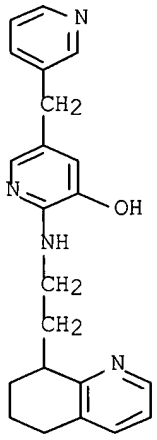


RN 112860-54-5 CAPLUS

CN 3-Pyridinol, 2-[[3-(5-bromo-3-methyl-2-pyridinyl)propyl]amino]-5-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 112860-56-7 CAPLUS
CN 3-Pyridinol, 5-(3-pyridinylmethyl)-2-[[2-(5,6,7,8-tetrahydro-8-quinolinyl)ethyl]amino]- (9CI) (CA INDEX NAME)



=> s l4 not l5
L6 11 L4 NOT L5

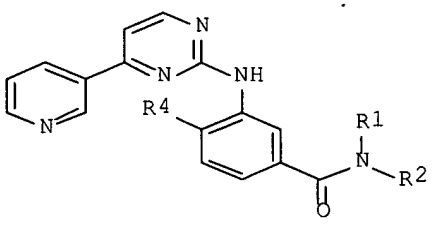
=> dis l6 1-11 bib abs fhitstr

L6 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:886963 CAPLUS Full-text
DN 145:299522
TI Pharmaceutical combination of Bcr-Abl and RAF inhibitors
IN Manley, Paul W.
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 31pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006089781	A1	20060831	WO 2006-EP1740	20060224

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,

VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI US 2005-656340P P 20050225
OS MARPAT 145:299522
GI

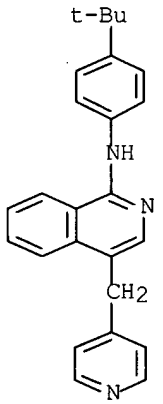


I

AB The invention provides a pharmaceutical combination comprising: (a) a pyrimidylaminobenzamide compound, and (b) a RAF kinase inhibitor and a method for treating or preventing a proliferative disease using such a combination, wherein compound (a) has the following general Formula: (I), with R1, R2, and R4 defined in claims.

IT 258851-00-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combination of Bcr-Abl and RAF inhibitors)

RN 258851-00-2 CAPLUS
CN 1-Isoquinolinamine, N-[4-(1,1-dimethylethyl)phenyl]-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:513675 CAPLUS Full-text
DN 145:34151

TI Combinations of JAK kinase inhibitors
IN Cooke, Nigel Graham; Manley, Paul W.
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006056399	A2	20060601	WO 2005-EP12480	20051122
WO 2006056399	A3	20060831		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

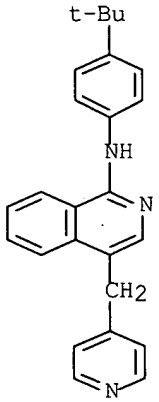
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2004-630713P P 20041124

AB The invention provides a pharmaceutical combination comprising (a) at least one agent selected from Bcr-Abl, Flt-3, FAK and RAF kinase inhibitors; and (b) at least one JAK kinase inhibitor, and a method for treating or preventing a proliferative disease using such a combination. A preferred embodiment of the invention is the combination of a RAF inhibitor, e.g., (4-tert-butylphenyl)-(4-pyridin-4-yl-methyl-isoquinolin-1- yl)amine or [4,7']bi-isoquinolinyl-1-yl-4-(tert-butylphenyl)amine, and a JAK kinase inhibitor, such as PNU 156804 or WHI-P 131 for the treatment of myelomas, especially multiple myeloma.

IT 258851-00-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of JAK kinase inhibitors with other protein kinase inhibitors for treatment or prevention of proliferative disease)

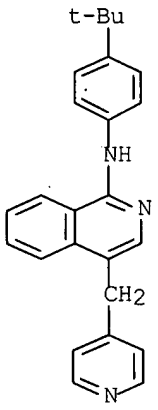
RN 258851-00-2 CAPLUS
CN 1-Isoquinolinamine, N-[4-(1,1-dimethylethyl)phenyl]-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:878558 CAPLUS Full-text
DN 141:360667
TI Methods for treating and diagnosing diseases having an aberrant MAP kinase signaling pathway, such as proliferative diseases, and for monitoring the effectiveness of treatment of proliferative diseases
IN Hu, Ping; Wang, Yingqi Karen; Batt, David Bryant
PA Novartis Ag, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004090545	A2	20041021	WO 2004-EP3877	20040413
	WO 2004090545	A3	20050811		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004227103	A1	20041021	AU 2004-227103	20040413
	CA 2522333	A1	20041021	CA 2004-2522333	20040413
	EP 1616191	A2	20060118	EP 2004-726981	20040413
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	BR 2004009409	A	20060425	BR 2004-9409	20040413
	CN 1784602	A	20060607	CN 2004-80011895	20040413
	JP 2006525962	T	20061116	JP 2006-505103	20040413
PRAI	US 2003-462723P	P	20030414		
	WO 2004-EP3877	W	20040413		

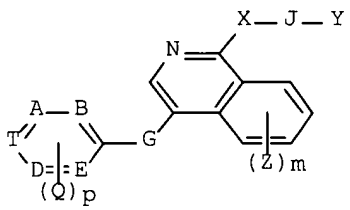
AB The present invention relates to phosphoproteins useful as biomarkers for identifying and treating patients suffering from diseases characterized by an aberrant MAP kinase signaling pathway, for example proliferative diseases like certain cancers, monitoring the efficacy of treatment of patients having the disease by administering Raf kinase inhibitors and diagnosing the disease in patients.
IT 258851-00-2, BPMI
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Raf inhibitor; phosphoproteins as biomarkers in treatment and diagnosis of diseases having aberrant MAP kinase signaling pathway, such as proliferative diseases, and for monitoring treatment effectiveness)
RN 258851-00-2 CAPLUS
CN 1-Isoquinolinamine, N-[4-(1,1-dimethylethyl)phenyl]-4-(4-pyridinylmethyl)-(9CI) (CA INDEX NAME)



L6 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:780541 CAPLUS Full-text
DN 141:295873
TI Preparation of N-aryl (heteroarylalkyl)isoquinolineamines as inhibitors of mutant and wild-type MAP kinases for the treatment of cancer
IN Batt, David Bryant; Bold, Guido; Kim, Sunkyu; Ramsey, Timothy Michael; Sabio, Michael Lloyd
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004080464	A1	20040923	WO 2004-EP2460	20040310
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004218914	A1	20040923	AU 2004-218914	20040310
	CA 2518530	A1	20040923	CA 2004-2518530	20040310
	EP 1603566	A1	20051214	EP 2004-718960	20040310
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
	BR 2004008257	A	20060307	BR 2004-8257	20040310
	CN 1758910	A	20060412	CN 2004-80006570	20040310
	JP 2006519807	T	20060831	JP 2006-504625	20040310
	NO 2005004647	A	20051209	NO 2005-4647	20051010
PRAI	US 2003-453624P	P	20030311		
	WO 2004-EP2460	A	20040310		

OS MARPAT 141:295873
GI



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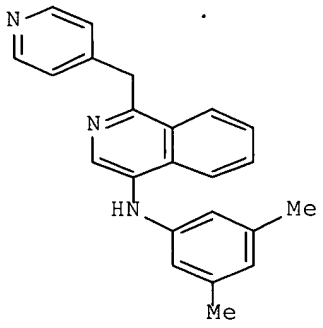


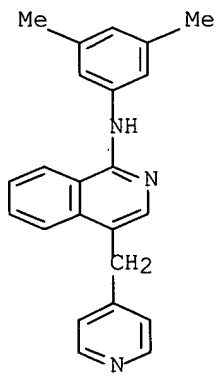
II

AB Compds. I [A, B, D, E, T = CH, N (independent; between one and three of A, B, D, E, or T are N); G = alkylene, CH2O, CH2S, CH2NH, SO2, O, S, NR; J = (CHR)n; R = H, alkyl; X = Y, RN, O, S; Y = H, (un)substituted alkyl, aryl, heteroaryl, cycloalkyl; Z = halogen, hydroxy, nitro, cyano, carboxy, (un)substituted amino, alkoxy, alkylcarbonyloxy, alkoxycarbonyl, etc.; m = 0-4; n, p = 0-2], particularly N-aryl (azaheteroarylalkyl)isoquinolineamin es such as II, are prepared as inhibitors of MAP kinases for use in the treatment of cancers; I are especially useful in the treatment of cancers possessing mutant Raf kinases, such as melanoma. 2-(Cyanomethyl)benzoic acid is esterified with DMF di-Me acetal to give its Me ester which undergoes condensation with 4-pyridinecarboxaldehyde followed by reesterification of the benzoic acid to yield 2-(2-methoxycarbonylphenyl)- 3-(4-pyridinyl)acrylonitrile (III); hydrogenation and concomitant cyclocondensation of III yields 4-(4-pyridylmethyl)-1-isoquinolinone which is then chlorinated to yield 1-chloro-4-(4-pyridinylmethyl)isoquinoline (IV). Condensation of IV with 3,5-dimethylaniline yields II. Compds. of the invention inhibit either wild-type C-Raf with IC50 values between 0.01 μM and 3.5 μM, wild-type B-Raf with IC50 values between 0.03 μM and 3.7 μM, or a mutant B-Raf (V599E) with IC50 values between 0.01 μM and 3.4 μM (no data).

IT 258850-90-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of mutant and wild-type MAP kinase-inhibiting N-aryl (heteroarylalkyl)isoquinolineamines as potential anticancer agents)

RN 258850-90-7 CAPLUS

CN 1-Isoquinolinamine, N-(3,5-dimethylphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)

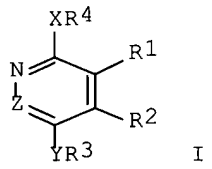


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:113527 CAPLUS Full-text
DN 140:163891
TI Preparation of substituted pyridines and pyridazines with angiogenesis inhibiting activity for pharmaceutical use as antitumor agents
IN Dumas, Jacques P.; Boyer, Stephen James; Dixon, Julie A.; Joe, Teddy Kite; Kluender, Harold C. E.; Lee, Wendy; Nagarathnam, Dhanapalan; Sibley, Robert N.; Su, Ning
PA Bayer Pharmaceuticals Corporation, USA
SO U.S., 60 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6689883	B1	20040210	US 2000-672294	20000928
	US 2004092740	A1	20040513	US 2003-720702	20031124
PRAI	US 1999-287595P	P	19990928		
	US 2000-672294	A3	20000927		

OS MARPAT 140:163891
GI



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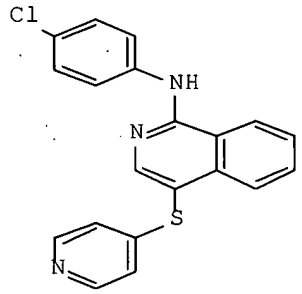


II

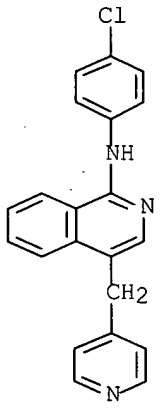
AB Fused ring systems with a pyridine or pyridazine subunit, such as I [X = connecting group, such as O, S, NH, etc.; Y = connecting group, such as O, S, CH2O, CH2S, NH, OCH2, SCH2, SO, SO2, etc.; Z = CH, N; R1R2 = fused ring, such as CH:CHCH:CH, CH:CHS, CH:CHO, CH:CHNH, N:CHNH, N:NNH, etc.; R3, R4 = aryl, heteroaryl, etc.; XR4 = nitrogen bound heterocyclyl, such as 1-indolinyl], with angiogenesis inhibiting activity were prepared for pharmaceutical use as antitumor agents. Thus, substituted isoquinoline II was prepared in a 3 step sequence which included bromination of isocarbostyril to form 1,4-dibromoisoquinoline in 96% yield, followed by monoamination with 4-chloroaniline to give 4-bromo-N-(4-chlorophenyl)-1- isoquinolinamine in 64.4% yield, and subsequent reaction with 4-mercaptopyridine to give II in 19% yield. The prepared compds. were tested for KDR receptor inhibition.

IT 258850-91-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted pyridines and pyridazines with angiogenesis inhibiting activity for pharmaceutical use as antitumor agents)

RN 258850-91-8 CAPLUS

CN 1-Isoquinolinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:570820 CAPLUS Full-text

DN 139:111640

TI Anti-angiogenesis combination therapies using KDR inhibitor pyridazine or pyridine derivatives

IN Adams, Paul E.; Boyer, Stephen J.; Dumas, Jacques; Elting, James J.; Kluender, Harold C. E.

PA Bayer Corporation, USA; Bayer Pharmaceuticals Corporation

SO PCT Int. Appl., 127 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003059354	A2	20030724	WO 2002-US41145	20021220
	WO 2003059354	A3	20031113		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2471314	A1	20030724	CA 2002-2471314	20021220
	AU 2002364102	A1	20030730	AU 2002-364102	20021220
	EP 1467736	A2	20041020	EP 2002-798573	20021220
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

	JP 2006503796	T	20060202	JP 2003-559516	20021220
	US 2005019424	A1	20050127	US 2004-498935	20040616
PRAI	US 2001-344294P	P	20011221		
	WO 2002-US41145	W	20021220		

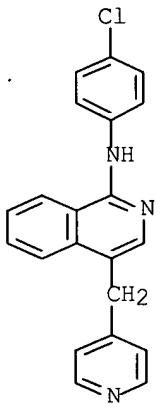
OS MARPAT 139:111640

AB The invention discloses the use of substituted fused or unfused pyridazine or pyridine derivs. which are KDR inhibitors in combination with other chemotherapeutic agents for use in treatment of diseases associated with abnormal angiogenesis and/or hyperpermeability and/or hyperproliferative diseases, e.g. cancer.

IT 258850-91-8
RL: PAC (Pharmacological activity); BIOL (Biological study)
(anti-angiogenesis combination therapies using KDR inhibitor pyridazine or pyridine derivs.)

RN 258850-91-8 CAPLUS

CN 1-Isoquinolinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:851122 CAPLUS Full-text

DN 135:371759

TI Preparation of N-imidazolylphenyl-5,6-dihydrobenzo[h]quinazolin-4-amines and other N-containing heterocyclic amines as 5-hydroxytryptamine antagonists for treatment of CNS disorders

IN Yamada, Akira; Spears, Glen; Hayashida, Hisashi; Tomishima, Masaki; Ito, Kiyotaka; Imanishi, Masashi

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 154 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

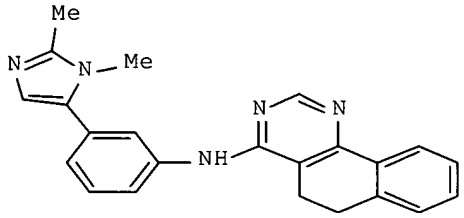
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001087845	A2	20011122	WO 2001-JP4002	20010514
WO 2001087845	A3	20020829		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,

SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	AU 2001056728	A5	20011126	AU 2001-56728	20010514
	US 2003176454	A1	20030918	US 2002-258582	20021101
PRAI	AU 2000-7501	A	20000515		
	AU 2000-1955	A	20001207		
	WO 2001-JP4002	W	20010514		

OS MARPAT 135:371759
GI



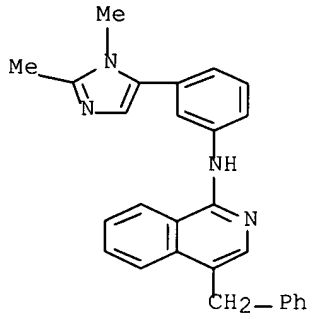
II

AB Title compds. AMQNHZ [I; wherein A = H, (un)substituted, unsatd., N-containing heterocyclic group, or C(NH)NHR; R = (un)substituted aryl or heterocyclic group; M = (CH2)n, (CH2)nO(CH2)m, or (CH2)nNH(CH2)m; n and m = independently 0-2; Q = (un)substituted cycloalkylene group, arylene, or divalent heterocyclic group; Z = (un)substituted, unsatd., mono-, di-, tri-, or tetracyclic, N-containing heterocyclic group which may contain addnl. N, O, and S atoms as the ring member(s), e.g. indeno[1,2,3- de]phthalazinyl or 5,6-dihydrobenzo[h]quinazolinyl; and the prodrugs or pharmaceutically acceptable salts thereof] were prepared For example, a mixture of 4-chloro-5,6-dihydrobenzo[h]quinazoline, 3-(1,2-dimethyl-1H- imidazol-5-yl)aniline, and 1,3-dimethyl-2-imidazolidinone was heated for an hour at 200°C, cooled, treated with 1N aqueous NaOH and water, and worked up to give II. I are 5-hydroxytryptamine (5-HT) antagonists useful for the prevention and/or treatment of central nervous system (CNS) disorders, such as anxiety, depression, obsessive compulsive disorders, migraine, anorexia, Alzheimer's disease, sleep disorders, bulimia, panic attacks, withdrawal from drug abuse, schizophrenia, and disorders associated with spinal trauma and/or head injury (no data).

IT 374556-53-3P, 4-Benzyl-N-[3-(1,2-dimethyl-1H-imidazol-5-yl)phenyl]-1-isoquinolinamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-(imidazolylphenyl)dihydrobenzo[h]quinazolinamines and other N-containing heterocyclic amines as 5-hydroxytryptamine antagonists for treatment of CNS disorders)

RN 374556-53-3 CAPLUS

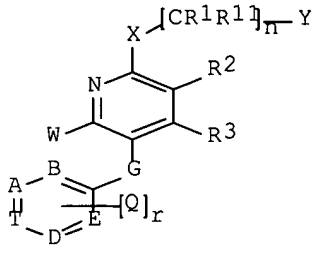
CN 1-Isoquinolinamine, N-[3-(1,2-dimethyl-1H-imidazol-5-yl)phenyl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:597986 CAPLUS Full-text
DN 135:180710
TI Preparation of isoquinolinamines inhibiting angiogenesis and/or VEGF receptor tyrosine kinase
IN Bold, Guido; Manley, Paul William
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001058899	A1	20010816	WO 2001-EP1331	20010207
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001031710	A5	20010820	AU 2001-31710	20010207
	EP 1254138	A1	20021106	EP 2001-903716	20010207
	EP 1254138	B1	20050511		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003522773	T	20030729	JP 2001-558449	20010207
	AT 295365	T	20050515	AT 2001-903716	20010207
	PT 1254138	T	20050930	PT 2001-903716	20010207
	ES 2241781	T3	20051101	ES 2001-1903716	20010207
	US 2003158409	A1	20030821	US 2002-203579	20021011
	US 6706731	B2	20040316		
	HK 1052500	A1	20060224	HK 2003-103231	20030506
	US 2004209894	A1	20041021	US 2004-766181	20040127
PRAI	CH 2000-265	A	20000209		
	WO 2001-EP1331	W	20010207		
	US 2002-203579	A1	20021011		

OS MARPAT 135:180710
GI



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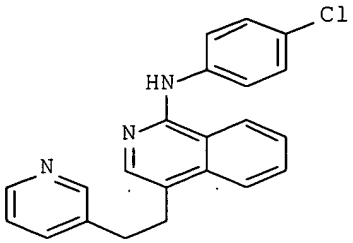


II

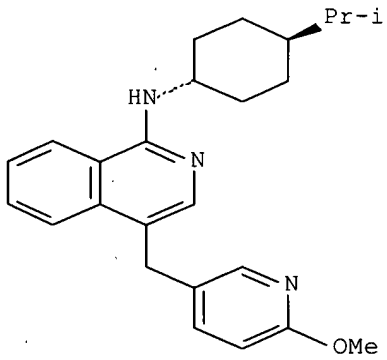
AB The title compds. [I; A, D, T = N, CH, CR4 (with the proviso that at least one of A and D = CR4 when T = N); R4 = alkyl, alkenyl, alkylthio, etc.; B, E = N, CH; G = alkylene, alkenylene, CH2OCH2, etc.; n = 0-2; Q = alkyl, whereby A, D and T are not substituted by Q if they represent CR4; r = 0-5; R1, R11 = H, alkyl; R2, R3 = alkyl; or R2 and R3 together form a bridge to form isoquinoline, naphthyridine, etc.; X = NR5, O, S; R5 = H, alkyl; Y = H, aryl, heterocyclyl, etc.], useful for the treatment of a disease which responds to an inhibition of angiogenesis, were prepared and formulated. E.g., a multi-step synthesis of II which showed IC50 of 0.105 μM against KDR VEGF-receptor tyrosine kinase, was given.

IT 355013-23-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of isoquinolinamines inhibiting angiogenesis and/or VEGF receptor tyrosine kinase)

RN 355013-23-9 CAPLUS

CN 1-Isoquinolinamine, 4-[(6-methoxy-3-pyridinyl)methyl]-N-[trans-4-(1-methylethyl)cyclohexyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:247328 CAPLUS Full-text

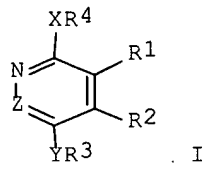
DN 134:266326

TI Preparation of substituted pyridines and pyridazines with angiogenesis inhibiting activity for pharmaceutical use as antitumor agents

IN Dumas, Jacques P.; Joe, Teddy Kite; Kluender, Harold C. E.; Lee, Wendy; Nagarathnam, Dhanapalan; Sibley, Robert N.; Su, Ning; Boyer, Stephen James; Dixon, Julie A.
PA Bayer Corporation, USA
SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001023375	A2	20010405	WO 2000-US26500	20000926
	WO 2001023375	A3	20020502		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	TW 593315	B	20040621	TW 2000-89119700	20000925
	CA 2385817	A1	20010405	CA 2000-2385817	20000926
	EP 1228063	A2	20020807	EP 2000-978215	20000926
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	HU 200202704	A2	20021228	HU 2002-2704	20000926
	BR 2000014382	A	20030624	BR 2000-14382	20000926
	EE 200200161	A	20030815	EE 2002-161	20000926
	JP 2003526632	T	20030909	JP 2001-526527	20000926
	NZ 518589	A	20050324	NZ 2000-518589	20000926
	AU 782820	B2	20050901	AU 2001-15696	20000926
	RU 2260008	C2	20050910	RU 2002-111414	20000926
	CN 1769282	A	20060510	CN 2005-10127109	20000926
	CN 1769283	A	20060510	CN 2005-10127110	20000926
	NO 2002001520	A	20020523	NO 2002-1520	20020326
	ZA 2002002760	A	20030818	ZA 2002-2760	20020409
	IN 2002MN00458	A	20050318	IN 2002-MN458	20020412
	BG 106637	A	20030228	BG 2002-106637	20020423
PRAI	US 1999-407600	A	19990928		
	CN 2000-816369	A3	20000926		
	WO 2000-US26500	W	20000926		

OS MARPAT 134:266326
GI



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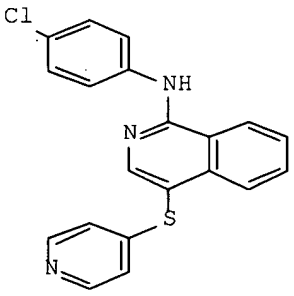


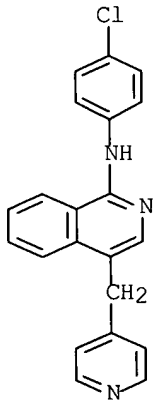
II

AB Fused ring systems with a pyridine or pyridazine subunit, such as I [X = connecting group, such as O, S, NH, etc.; Y = connecting group, such as O, S, CH2O, CH2S, NH, OCH2, SCH2, SO, SO2, etc.; Z = CH, N; R1R2 = fused ring, such as CH:CHCH:CH, CH:CHS, CH:CHO, CH:CHNH, N:CHNH, N:NNH, etc.; R3, R4 = aryl, heteroaryl, etc.; XR4 = nitrogen bound heterocyclyl, such as 1-indolinyl], with angiogenesis inhibiting activity were prepared for pharmaceutical use as antitumor agents. Thus, substituted isoquinoline II was prepared in a 3 step sequence which included bromination of isocarbostyril to form 1,4-dibromoisoquinoline in 96% yield, followed by monoamination with 4-chloroaniline to give 4-bromo-N-(4-chlorophenyl)-1- isoquinolinamine in 64.4% yield, and subsequent reaction with 4-mercaptopyridine to give II in 19% yield. The prepared compds. were tested for KDR receptor inhibition.

IT 258850-91-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted pyridines and pyridazines with angiogenesis inhibiting activity for pharmaceutical use as antitumor agents)

RN 258850-91-8 CAPLUS

CN 1-Isoquinolinamine, N-(4-chlorophenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:31464 CAPLUS Full-text

DN 134:100762

TI Preparation of pyridine derivatives and medicinal use thereof

IN Iino, Yukio; Fujita, Kohichi; Kodaira, Ariko; Hatanaka, Toshihiro; Takehana, Kenji; Kobayashi, Tsuyoshi; Konishi, Atsushi; Yamamoto, Takashi

PA Ajinomoto Co., Inc., Japan

SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001002359	A1	20010111	WO 2000-JP4298	20000629

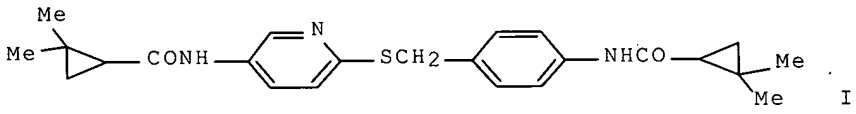
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2377771	A1	20010111	CA 2000-2377771		20000629
EP 1193255	A1	20020403	EP 2000-940879		20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 2000012046	A	20020514	BR 2000-12046		20000629
TW 519538	B	20030201	TW 2000-89113050		20000630
US 2002133005	A1	20020919	US 2001-29871		20011231
US 6794378	B2	20040921			
PRAI JP 1999-187959	A	19990701			
JP 2000-71706	A	20000315			
WO 2000-JP4298	W	20000629			

OS MARPAT 134:100762

GI



I

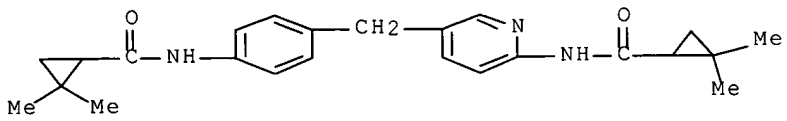
AB Heterocyclic compds. represented by the following general formula R1-CO-N(R2)-A-X-B-N(R3)-Y-(CH2)n-R4 [R1 = (un)substituted or cycloalkenyl; R2, R3 = H, alkyl; R4 = (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, or heterocyclyl having ≥1 heteroatom(s); A = (un)substituted heterocyclic ring; B = (un)substituted aromatic or heterocyclic ring; n = 0-6; Y = a bond between atoms, CO, CO2, CONR5, C(S)NR5, SO, SO2 (wherein R5 = H, alkyl); X = a bond between atoms, O, OCHR7, CHR8O, O2C, CO2, OC(S), C(S)O, S, SO, SO2, SCHR9, CHR10S, SC(O), C(O)S, SC(S), C(S)S, SO2 NR11, NR12SO2, NR13, etc.; R7 - R10 = H, alkyl; R11 - R13 = H, alkyl, acyl] or pharmacol. acceptable salts thereof are prepared These compds. have inhibitory effects on AP-1 activity, NF-kappa B activity, inflammatory cytokine production, matrix metalloprotease production, expression of inflammatory cell adhesion factor, etc. and are usable as drugs such as antiinflammatory, antirheumatic, antiviral agents, immunosuppressants, cancer metastasis inhibitors, and antiarteriosclerotics. Thus, 2-mercapto-5-nitropyridine was treated with NaH in DMF and then alkylated by 1-bromomethyl-4-nitrobenzene at room temperature for 1.5 h to give 2-(4-nitrobenzylthio)-5-nitropyridine which was reduced by Zn/AcOH in THF at room temperature for 16 h to 2-(4-aminobenzylthio)- 5-aminopyridine and then acylated by 2,2-dimethylcyclopropanecarbonyl chloride in the presence of Et3N in CH2Cl2 at room temperature for 17 h to give 2-(4-(2,2-dimethylcyclopropanecarbonylamino)benzylthio)-5-(2,2-dimethylcyclopropanecarbonylamino)pyridine (I). I in vitro inhibited NF-kappa B activity with IC50 of 0.015 μg/mL in an assay measuring β-galactosidase activity expressed in HUVEC cells and driven by NF-kappa B-binding sequence-fused SV40 T antigen min. promoter.

IT 318967-18-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyridine derivs. as inhibitors of AP-1 activity, NF-kappa B activity, inflammatory cytokine production, matrix metalloprotease production,
expression of inflammatory cell adhesion factor)

RN 318967-18-9 CAPLUS

CN Cyclopropanecarboxamide, N-[5-[[4-[[(2,2-dimethylcyclopropyl)carbonyl]amino]phenyl]methyl]-2-pyridinyl]-2,2-dimethyl- (9CI) (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2000:133671 CAPLUS Full-text

DN 132:166131

TI Preparation of isoquinolines with angiogenesis inhibiting activity

IN Altmann, Karl-Heinz; Bold, Guido; Manley, Paul William

PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H

SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000009495	A1	20000224	WO 1999-EP5781	19990809
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2339961	A1	20000224	CA 1999-2339961	19990809
	AU 9956202	A1	20000306	AU 1999-56202	19990809
	BR 9912938	A	20010508	BR 1999-12938	19990809
	EP 1107964	A1	20010620	EP 1999-942827	19990809
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002522535	T	20020723	JP 2000-564947	19990809
	US 2002010181	A1	20020124	US 2001-781036	20010209
	US 6608071	B2	20030819		
PRAI	CH 1998-1654	A	19980811		
	WO 1999-EP5781	W	19990809		

OS MARPAT 132:166131

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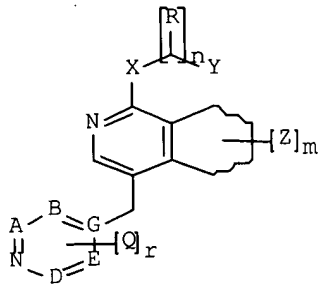

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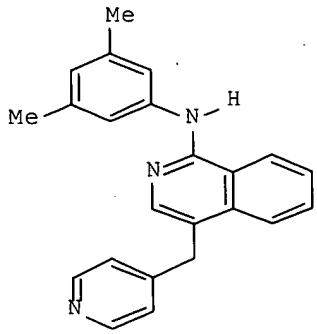


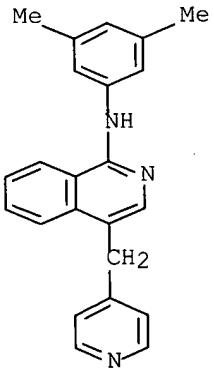
II

AB The title compds. [I; r = 0-2; n = 0-2; m = 0-4; A, B, D, E = N, CH (with the proviso that not more than two of those radicals are N); G = alkylene, CH2O, CH2S, etc.; Q = alkyl, especially methyl; R = H, alkyl; X = NH, O, S; Y = alkyl, especially, aryl, heteroaryl, (un)substituted cycloalkyl; Z = (un)substituted NH2, halo, alkyl, etc.; the bonds indicated by a wavy line are either single bonds or double bonds] which inhibit especially angiogenesis, were prepared and formulated. E.g., a multi-step synthesis of II which showed IC50 of 0.802 μM against Flt-1 VEGF receptor tyrosine kinase, was given.

IT 258850-90-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoquinolines with angiogenesis inhibiting activity)

RN 258850-90-7 CAPLUS

CN 1-Isoquinolinamine, N-(3,5-dimethylphenyl)-4-(4-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STN INTERNATIONAL LOGOFF AT 17:29:56 ON 20 MAR 2007